Using negative signal in mono-TI pulsed arterial spin labeling to outline pathological increases in arterial transit times

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Target audience : MR Physicists, computer scientists, medical doctors.

PURPOSE : The presence of unexpected negative perfusion estimates has been sparsely discussed in the ASL literature [2,3]. In the study of perfusion maps extracted from a single inversion time in ASL (mono-TI ASL), it is however common to deal with areas of significant negative signal. This is problematic since performing statistical analysis based on this data might therefore lead to inacurrate results. Though isolated negative values could be attributed to noise, clusters of significant negative signal should be explained by another phenomenon. Following [2], which outlined that negative values might arise due to increased transit times, we investigated this hypothesis based on real clinical datasets including healthy control and patient data.

METHODS : First, in a simulation, we studied how an increase in transit time can affect the perfusion-weighted estimate obtained in mono-TI PASL studies.

Second, on a dataset of 36 healthy subjects, we computed a one-sample t-test per voxel in order to outline significant negative signal ($p<0.05$ uncorrected). We then looked at the spatial distribution of negative perfusion estimates.

Third, on 2 patients diagnosed with brain tumors, we examined the location of significant negative signal in view of time to peak (TTP) maps extracted from dynamic susceptibility contrast (DSC) perfusion MRI.

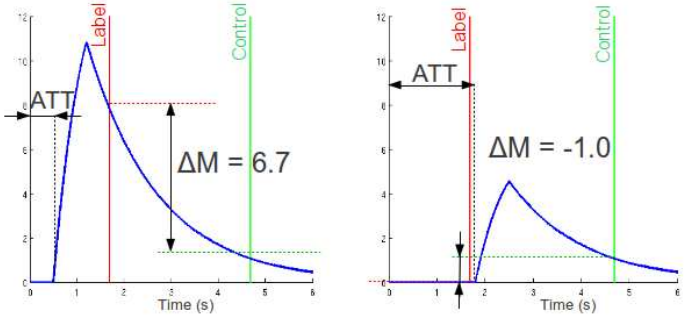

Figure 1: Perfusion signal against time. Increased ATT can lead to negative perfusion estimate.

RESULTS : Figure 1 displays the theoretical curve of the perfusion signal against time [1] with a realistic set of parameters. If the Arterial Transit Time (ATT) exceeds the inversion time minus the bolus width then the estimation of cerebral blood flow based on a single time point is no longer accurate and can even lead to negative perfusion estimates. In theory, given the presence of pre-saturation pulses, such a negative signal should not arise. We therefore wonder if the efficiency of pre-saturation pulse on the remaining perfusion signal is in question or if other effects can explain the presence of significatively negative signal.

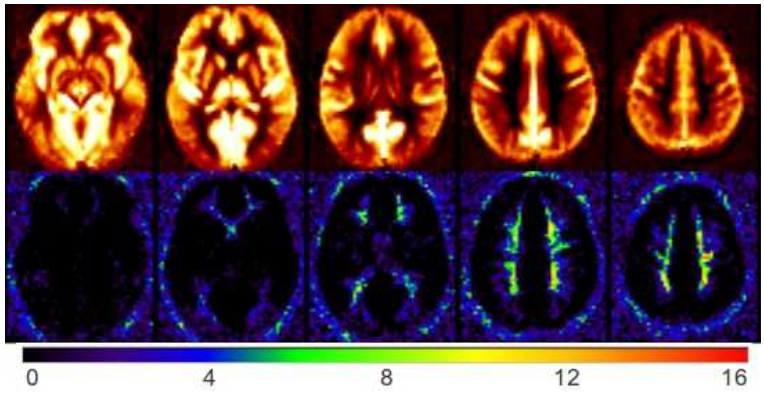

Figure 2: Mean perfusion signal, and number of subjects presenting negative signal in a dataset of 36 healthy controls

In Figure 2, the first row presents the average perfusion signal extracted from a dataset of 36 healthy subjects. On the second row, a map of the number of controls (out of 36) presenting significant negative signal is displayed. In healthy subject data, negative perfusion estimates are confined to deep white matter, which is the area of the brain known to have the longest transit time.

In Figure 3, the data of 2 patients diagnosed with brain tumors is presented. Areas of significant negative signal correspond to increased time to peak (TTP) as extracted from Dynamic Susceptibility Contrast (DSC).

DISCUSSION: Negative perfusion estimates are found in patient as well as control perfusion-weighted data extracted from mono-TI ASL data. In healthy subjects, where cardiac defect has to be excluded [3], longer ATT is the most probable explanation of large clusters of significant negative signal observable in deep white matter. In patients diagnosed with brain tumors, areas of significant negative signal are colocated with increased TTP.

CONCLUSION : Based on these results, we advise to systematically check for negative perfusion signal before computing any type of analysis based on mono-TI ASL perfusion maps. In pathological condition, areas outlined as significantly negative can indicate increased transit times.

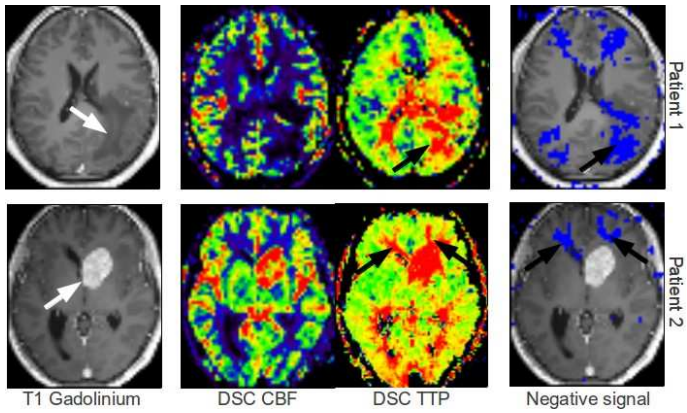

Figure 3 : Colocalisation of negative perfusion estimates and increased Time To Peak (TTP) in a dataset of 2 patients diagnosed with brain tumors.

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